ACC.12
61st Annual Scientific Session & Expo
ACC-i2 with TCT innovation in intervention

E729
JACC March 27, 2012
Volume 59, Issue 13

Arrhythmias

ORAL CONTRACEPTIVE USE AND CORRECTED QT INTERVAL: EVIDENCE OF AN ADVERSE EFFECT

ACC Moderated Poster Contributions
McCormick Place South, Hall A
Monday, March 26, 2012, 11:00 a.m.-Noon

Session Title: Arrhythmias: Advances that Impact Sudden Cardiac Death
Abstract Category: 20. Arrhythmias: Other
Presentation Number: 1249-636

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Background: A prolonged corrected QT (QTc) interval is a marker for an increased risk of sudden cardiac death. Prior studies have shown that while testosterone and progesterone shorten the action potential, estrogen lengthens the QTc interval. We evaluated the relationship between oral contraceptive (OC) use, type of OC, and QTc interval in a managed care population.

Methods: We retrospectively identified 410,782 12-lead surface ECGs performed at Northern California Kaiser Permanente on female patients between 15-53 years as part of clinical care from January, 1995 to June, 2008. Machine-read raw QT was corrected for heart rate using log-linear regression. OC generation (first, second and third) was classified by increasing progestin androgenic potency, while the fourth generation was classified as anti-androgenic. Statistical analysis was performed using multivariable linear regression adjusting for age, race, smoking and comorbidity.

Results: Among 410,782 women, 8.4% were on OC. Women taking OC were younger (33.2 vs 40.7 years) and had less comorbidity than unexposed women ($p<0.0001$). Overall, exposed women had a shorter QTc (400.8 msec) than unexposed women (403.5 msec) ($p<0.0001$). In multivariate analysis, there was an independent shortening effect of OCs overall (slope = -0.5ms; SE = 0.12, $p<0.0002$). When examined by OC generation, users of first and second generation progestins had a significantly shorter QTc than non-users (first generation: slope = -1.0ms, SE = 0.18, $p<0.0001$; second generation: slope = -2.0ms, SE = 0.23, $p<0.0001$) while users of fourth generation had a significantly longer QTc than non-users (slope = 3.6ms, SE = 0.35, $p<0.0001$).

Conclusion: Overall, OC use has a small but significant shortening effect on the QTc. OC generation is an important predictor of QTc length after adjusting for age and comorbidity, with shorter QTc seen with first and second generation OC. Fourth generation OC use with anti-androgenic progestin has a lengthening effect on the QTc. As even small QTc prolongation can be clinically relevant, particularly when combined with other factors and QTc prolonging medications, careful examination of adverse event rates in fourth generation OC users is needed.